Supplementary Information

Supplementary Table 1. PNA-RNA duplex models with corresponding melting temperatures measured by CD.

Duplex	Sequence label	Sequence*	T_m, °C†
1	pD12	N-SBTG$_2$-DAP-AEEA-GCCA**T**CAGCTCC-AEEA-D(Cys-Ser-Lys-Cys)-C	79 ± 1.0
	mD12	5'-rAGUUGGAGCUG**A**UGGCGUAG-3'	
2	pD12	N-SBTG$_2$-DAP-AEEA-GCCA**T**CAGCTCC-AEEA-D(Cys-Ser-Lys-Cys)-C	65 ± 1.7
	mG12	5'-rAGUUGGAGCUG**G**UGGCGUAG-3'	
3	pG12	N-SBTG$_2$-DAP-AEEA-GCCA**C**CAGCTCC-AEEA-D(Cys-Ser-Lys-Cys)-C	82 ± 1.0
	mG12	5'-rAGUUGGAGCUG**G**UGGCGUAG-3'	
4	pG12	N-SBTG$_2$-DAP-AEEA-GCCA**C**CAGCTCC-AEEA-D(Cys-Ser-Lys-Cys)-C	66 ± 0.9
	mV12	5'-AGUUGGAGCUG**U**UGGCGUAG-3'	
5	pG12	N-SBTG$_2$-DAP-AEEA-GCCA**C**CAGCTCC-AEEA-D(Cys-Ser-Lys-Cys)-C	67 ± 1.1
	mD12	5'-rAGUUGGAGCUG**A**UGGCGUAG-3'	
6	pV12	N-SBTG$_2$-DAP-AEEA-GCCA**A**CAGCTCC-AEEA-D(Cys-Ser-Lys-Cys)-C	78 ± 0.6
	mV12	5'-AGUUGGAGCUG**U**UGGCGUAG-3'	
7	pV12	N-SBTG$_2$-DAP-AEEA-GCCA**A**CAGCTCC-AEEA-D(Cys-Ser-Lys-Cys)-C	69 ± 0.3
	mG12	5'-rAGUUGGAGCUG**G**UGGCGUAG-3'	
8	pDVA12	N-SBTG$_2$-DAP-AEEA-GCCA**H**CAGCTCC-AEEA-D(Cys-Ser-Lys-Cys)-C	72 ± 0.9
	mD12	5'-rAGUUGGAGCUG**A**UGGCGUAG-3'	
9	pDVA12	N-SBTG$_2$-DAP-AEEA-GCCA**H**CAGCTCC-AEEA-D(Cys-Ser-Lys-Cys)-C	66 ± 3.5
	mG12	5'-rAGUUGGAGCUG**G**UGGCGUAG-3'	
10	pDVA12	N-SBTG$_2$-DAP-AEEA-GCCA**H**CAGCTCC-AEEA-D(Cys-Ser-Lys-Cys)-C	72 ± 0.5
	mV12	5'-AGUUGGAGCUG**U**UGGCGUAG-3'	

*The position of mutation in the twelfth codon (underlined) is colored red. †T_m values were calculated from the first derivative of the melting curve.

Supplementary Table 2. Average values helical parameters PNA-RNA duplexes calculated over 25.0 ns MD simulations. The error values represent the standard error.

Duplex	Helical Twist (º)	Helical Rise (Å)	Shift (Å)	Slide (Å)	Rise (Å)	Tilt (º)	Roll (º)	Twist (º)
pD12-mD12	26.1 ± 4	2.76 ± 0.4	0.55 ± 0.6	−2.03 ± 0.5	3.31 ± 0.4	−0.22 ± 4.7	5.63 ± 5.8	25.3 ± 4.2
pD12-mG12	26.6 ± 6	2.71 ± 0.4	0.53 ± 0.6	−2.02 ± 0.5	3.27 ± 0.3	0.26 ± 4.9	6.01 ± 5.9	25.7 ± 6.3
pG12-mG12	25.9 ± 4	2.74 ± 0.4	0.54 ± 0.6	−2.11 ± 0.4	3.31 ± 0.3	−0.54 ± 4.6	5.43 ± 5.6	25.1 ± 4.4
pG12-mD12	25.2 ± 9	2.58 ± 07	0.63 ± 0.8	−2.07 ± 0.6	3.33 ± 0.5	−1.36 ± 5.7	5.95 ± 6.5	23.9 ± 10
pG12-mV12	26.8 ± 9	2.58 ± 0.6	0.55 ± 0.6	−1.97 ± 0.5	3.29 ± 0.4	−1.29 ± 5.9	6.67 ± 6.4	25.5 ± 10
pV12-mV12	25.9 ± 4	2.77 ± 0.5	0.56 ± 0.7	−2.00 ± 0.5	3.32 ± 0.4	−0.38 ± 5.0	5.75 ± 6.0	25.1 ± 4.9
pV12-mG12	25.8 ± 15	2.44 ± 0.9	0.64 ± 1.0	−1.93 ± 0.9	3.30 ± 0.4	−1.20 ± 5.8	7.21 ± 6.6	24.1 ± 15
pDVA12-mD12	26.1 ± 5	2.68 ± 0.6	0.56 ± 0.9	−2.00 ± 0.7	3.33 ± 0.4	−0.43 ± 5.7	6.43 ± 6.4	24.3 ± 9.6
pDVA12-mG12	23.2 ± 17	2.65 ± 1.2	0.70 ± 1.6	−2.02 ± 1.3	3.39 ± 1.2	−0.12 ± 11	6.27 ± 10	21.9 ± 16
pDVA12-mV12	26.7 ± 7	2.67 ± 0.5	0.55 ± 0.6	−1.95 ± 0.5	3.30 ± 0.4	−0.56 ± 5.3	6.59 ± 6.3	25.6 ± 7.4

Supplementary Table 3. MM-PBSA results for each PNA-RNA duplex using the last 6ns of each 25 ns MD simulation. Errors represent the standard deviation of 3 independent MD runs.

Duplex	ΔE^{ele}*	ΔE^{vdW}**	ΔG^{PB}***	ΔG^{SA}****	$\Delta H^{MM\text{-}PBSA}$	$T\Delta S$	ΔG^{calc}	T_m^{calc}	T_m^{exp}
pD12-mD12	-131.8 ± 1.0	-70.7 ± 1.0	79.5 ± 10	-6.19 ± 0.0	-129.2 ± 1.0	-46.7 ± 1.8	-82.5 ± 2.4	696	352 ± 1.0
pG12-mG12	-160.0 ± 9.4	-70.9 ± 0.5	102.2 ± 8.9	-6.26 ± 0.0	-134.9 ± 1.1	-50.3 ±1.6	-84.7 ± 2.7	683	356 ± 1.0
pG12-mD12	-141.3 ± 11	-71.7 ± 0.7	90.3 ± 11	-6.29 ± 0.0	-129.0 ± 0.6	-47.8 ±1.4	-81.3 ± 1.9	682	341 ± 1.0
pV12-mV12	-146.2 ± 7.2	-69.7 ± 0.3	93.3 ± 6.4	-6.19 ± 0.0	-128.7 ± 0.6	-47.9 ±2.9	-80.8 ± 3.1	679	351 ± 0.6
pDVA12-mD12	-138.8 ± 8.7	-70.4 ± 1.9	88.9 ± 12	-6.25 ± 0.2	-126.6 ± 2.4	-42.2 ± 1.8	-84.5 ± 3.7	744	345 ± 0.9
pDVA12-mG12	-136.16 ± 26	-71.5 ± 1.3	91.7 ± 20	-6.52 ± 0.3	-118.8 ± 3.3	-44.9 ± 1.7	-73.8 ± 4.0	661	339 ± 3.5
pDVA12-mV12	-139.64 ± 16	-70.3 ± 0.8	87.8 ± 16	-6.18 ± 0.1	-128.3 ± 0.6	-44.2 ±2.0	-84.2 ± 2.4	725	346 ± 0.5

All energy units are given in kcal/mol, Temperatures are in K.

* ΔE^{ele} : Coulombic energy.

** ΔE^{vdW}: van der Waals energy.

*** ΔG^{PB}: Poisson-Boltzmann polar solvation energy

**** ΔG^{SA}: non-polar solvation energy

Supplementary Table 4. . MM-PBSA results for each PNA-RNA duplex using the 50ns of each aMD simulation.

Duplex	ΔE^{ele}*	ΔE^{vdW}**	ΔG^{PB}***	ΔG^{SA}****	$\Delta H^{MM-PBSA}$	$T\Delta S$	ΔG^{calc}	T_m^{calc}	T_m^{exp}
pD12-mD12	-130.9	-75.1	91.4	-6.6	-121.2	-46.11	-75.2	660	352 ± 1.0
pG12-mG12	-162.8	-71.0	113.8	-6.3	-126.4	-44.75	-81.6	706	356 ± 1.0
pG12-mD12	-260.9	-84.5	251.7	-7.5	-101.3	-39.5	-61.8	627	341 ± 1.0
pV12-mV12	-193.5	-72.9	156.1	-6.6	-116.9	-44.32	-72.5	658	351 ± 0.6
pDVA12-mD12	-149.0	-82.55	122.1	-7.5	-116.9	-45.69	-71.3	642	345 ± 0.9
pDVA12-mG12	-152.4	-77.4	122.0	-6.8	-114.6	-47.83	-66.8	605	339 ± 3.5
pDVA12-mV12	-145.9	-69.7	99.5	-6.2	-122.3	-46.63	-75.7	660	346 ± 0.5

All energy units are given in kcal/mol, Temperatures are in K.

* ΔE^{ele} : Coulombic energy.

** ΔE^{vdW}: van der Waals energy.

*** ΔG^{PB}: Poisson-Boltzmann polar solvation energy

**** ΔG^{SA}: non-polar solvation energy

Supplementary Table 5. Average values helical parameters PNA-RNA duplexes calculated over 50.0 ns aMD simulations. The error values represent the standard deviation.

Duplex	Helical Twist (º)	Helical Rise (Å)	Shift (Å)	Slide (Å)	Rise (Å)	Tilt (º)	Roll (º)	Twist (º)
pD12-mD12	26.4 ± 5.0	2.77 ± 0.3	0.57 ± 0.1	-1.93 ± 0.4	2.77 ± 0.3	-0.61 ± 1.6	6.03 ± 2.9	25.4 ± 5.3
pG12-mG12	26.8 ± 1.6	2.69 ± 0.1	0.51 ± 0.1	-1.94 ± 0.2	2.69 ± 0.1	-0.78 ± 1.4	6.75 ± 2.6	25.6 ± 1.6
pG12-mD12	15.4 ± 13	1.1 ± 0.9	0.78 ± 0.4	-1.27 ± 1.2	1.10 ± 0.9	-7.56 ± 6.0	17.2 ± 10	10.5 ± 13
pV12-mV12	26.4 ± 4.0	2.59 ± 0.2	0.64 ± 0.2	-1.96 ± 0.2	2.59 ± 0.2	-2.29 ± 1.9	6.35 ± 1.9	24.8 ± 4.2
pDVA12-mD12	24.3 ± 5.8	2.97 ± 0.5	0.92 ± 0.1	-1.26 ± 0.6	2.97 ± 0.5	0.92 ± 4.6	7.53 ± 4.4	22.5 ± 6.6
pDVA12-mG12	24.4 ± 6.3	2.24 ± 0.5	0.81 ± 1.0	-1.61 ± 0.6	2.24 ± 0.5	0.58 ± 2.3	9.52 ± 3.7	21.5 ± 6.8
pDVA12-mV12	26.9 ± 6.1	2.76 ± 0.2	0.66 ± 0.3	-1.51 ± 0.3	2.76 ± 0.2	-0.46 ± 2.1	6.76 ± 3.1	25.7 ± 6.4

Supplementary Table 6. Average values of base and helical parameters of the 8th position and effects of hypoxanthine substitutions during 50.0 ns aMD simulations. The error values represent the standard deviation.

Duplex	Base pair at 8th position	Shear (Å)	Stretch (Å)	Opening (º)
pD12-mD12	T-A	-0.1 ± 0.01	0.03 ± 0.01	3.2 ± 0.3
pG12-mG12	C-G	0.0 ± 0.02	0.02 ± 0.01	0.9 ± 0.2
pG12-mD12	C-A	-1.9 ± 0.2	0.8 ± 0.3	20 ± 2.8
pG12-mV12	C-U	-2.9 ± 0.1	-1.7 ± 0.04	-1.6 ± 0.6
pV12-mV12	A-U	-0.0 ± 0.03	-0.0 ± 0.01	4.2 ± 0.3
pDVA12-mD12	H-A	2.0 ± 0.1	1.3 ± 0.05	-38 ± 1.5
pDVA12-mG12	H-G	1.3 ± 0.2	4.5 ± 0.04	58 ± 1.9
pDVA12-mV12	H-U	-2.4 ± 0.1	0.4 ± 0.01	4.2 ± 0.3